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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,514	01/23/2006	Linzhao Cheng	JHU1910-5	4565
28213	7590	11/19/2009	EXAMINER	
DLA PIPER LLP (US) 4365 EXECUTIVE DRIVE SUITE 1100 SAN DIEGO, CA 92121-2133			CROUCH, DEBORAH	
			ART UNIT	PAPER NUMBER
			1632	
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			11/19/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/533,514

**Applicant(s)**

CHENG, LINZHAO

**Examiner**

Deborah Crouch

**Art Unit**

1632

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-30 and 34-64 is/are pending in the application.
- 4a) Of the above claim(s) 34-51 and 57-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-30 and 52-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
- Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 6, 2009 has been entered. The amendment has been entered. 1-30 and 34-64 are pending. Claims 34-51 and 57-64 have been withdrawn from consideration as to a non-elected invention. Claims 1-30 and 52-56 are examined herein.

The rejection made in the office action mailed May 7, 2009 under 35 U.S.C. § 102/103 as being anticipated by or in the alternative obvious over Bongso et al is withdrawn.

The rejection made in the office action mailed May 7, 2009 under 35 U.S.C. 102(e) as being clearly anticipated by PgPub 20050037488 (Mitalipov) is withdrawn in view of applicant's amendments to the claims.

The rejection made in the office action mailed May 7, 2009 under 35 U.S.C. 103(a) as being unpatentable over U.S. PgPub 2005003748 (Mitalipov) in view of U.S. Patent 6,921,632 issued July 26, 2005 (Lim) is withdrawn

The rejection made in the office action mailed May 7, 2009 under 35 U.S.C. 102(b) as being clearly anticipated by over Xu et al. is withdrawn.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9, 18, 25 and 56 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Thomson et al., Science, 1998, Vol. 282, pp. 1145-1147, IDS filed 1/11/08, AA).

Thomson teaches isolated hES cells that have a normal, diploid karyotype and are passaged for at least 32 times (page 1144, col.2, line 19 to col. 3, line 5). Absent results or arguments to the contrary, all hES cells required, as an inherent property, either a feeder cell layer or feeder cell conditioned media, evidence by U.S. PgPub 2005003748 (Mitalipov), see citations below. The claims do not require the presence of the feeder cells, only that the hES cells depend on them for growth. In a side by side comparison, a patentable distinction could not be discerned between the claimed hES

cells and those of Thomson. Claims 18, 25 and 56 states "a culture of undifferentiated pluripotential hES cells prepared by," which does not provide a structural alteration to the hES cells. Thus, Thomson anticipates the claimed invention. In the alternative, as the hES cells of the claims and those of Thomson are not patentably distinct, any differences are obvious differences.

Applicant's arguments are directed to Bongso, now withdrawn. With regard to the new rejection over Thomson, Thomson teaches the limitations of a diploid karyotype and four passages. Thomson's use of MEF feeder cells does not negate the anticipatory nature of the teachings therein. The particular feeder cell chosen is not viewed as altering the structure of the claimed hES cells. Any such differences need to be presented in a declaration under 37 § 37 § CFR 1.132. The claims state the hES cells are dependent on an adult human feeder cells, but the adult human feeder cell is not required to be present in the claims. "Dependent on" is not a structural limitation to the hES cells. The ordinary artisan would have believed Thomson's hES cells would have been dependent on adult feeder cells since a common characteristic of all ES cells is feeder dependency for pluripotency and self-renewal.

Claims 10-17, 19-24, 26-30 and 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. PgPub 2005003748 (Mitalipov) and Thomson et al., Science, 1998, Vol. 282, pp. 1145-1147, IDS filed 1/11/08, AA) in view of WO00/029001 published May 25, 2000 (McIntosh).

Mitalipov teaches a culture of hES cells on immortalized human skin fibroblasts and method of obtaining an expanded population of undifferentiated pluripotential hES

cells comprising culturing the culture (parag. [0050], [0051] and [0146]-[0156]). The fibroblasts are adult feeder cells producing an ES cell-maintaining product of the supportive adult human feeder cells. Mitalipov also teaches the feeder cells can be used to produce conditioned media (parag. [0202]). Mitalipov teaches isolating hES cells so cultured for pluripotency markers (parag. [0155]). further, Mitalipov teaches subculturing hES cells on the fibroblast feeder cells (parag. [0154], lines 6-9).

Thomson teaches isolated hES cells that have a normal, diploid karyotype and are passaged for at least 32 times (page 1144, col.2, line 19 to col. 3, line 5). Thomson further teaches the cryopreservation of hES cells, and subsequently throwing and culturing the frozen cells to create a cell line (page 1144, col. 2, lines 19-22).

The cultures of Mitalipov and Thomson are suspension cultures and contain an hES cell-maintaining product of the feeder cells. Applicant should note the alternative language in claim 52 does not limit the claims to "absence of feeder cells."

McIntosh teaches fibroblast cell line 1087sk, ATCC CRL-2104 (page 11, lines 20-22). McIntosh further teaches the media from culturing the 1087sk cells was used to prepare conditioned media (page 13, lines 3-7).

Thus, at the time of the instant invention, it would have been obvious to prepare a culture of hES cells with CCD-1087sk adult human fibroblasts from breast, culture the culture, subculture the culture and isolate hES cells from the culture as taught by Mitalipov including the teaching the propagation of hES cells on skin fibroblast feeder cells and Thompson including teaching the culture of hES cells on mouse embryonic fibroblast cells, in view of McIntosh teaching CCD-1087sk human adult fibroblasts The

artisan would have known at the time of filing to obtain CCD-1087sk cells from the ATCC. The claims require growth on CCD-1087sk feeder cells. The claimed invention is a known method modified by an element from a known and predictable method.

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in *KSR* can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. \_\_\_, 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention." In the present situation, rationales A, B, E and G are applicable. In particular both *Mitalipov* and *Thomson* teach fibroblast feeder cells maintain pluripotency and self-renewal of hES cells, so the substitution of fibroblasts

isolate from breast skin would be an obvious substitution with a predictable outcome. Additionally, a fibroblast from breast skin is the same as a fibroblast from another tissue. A fibroblast is a matrix support cell found in all tissues of the body. As such a fibroblast from one tissue type would be expected to function the same as a fibroblast from a second tissue type. Thus, the teachings of the cited prior art in the obviousness rejection above provide the requisite teachings and motivations with a clear, reasonable expectation. The cited prior art meets the criteria set forth in both Graham and KSR.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/  
Primary Examiner, Art Unit 1632

November 18, 2009